



ALS2 gene

ALS2, alsin Rho guanine nucleotide exchange factor

Normal Function

The *ALS2* gene provides instructions for making a protein called alsin. Alsin is produced in a wide range of tissues, with highest amounts in the brain. This protein is particularly abundant in motor neurons, the specialized nerve cells in the brain and spinal cord that control the movement of muscles.

Alsin turns on (activates) multiple proteins called GTPases that convert a molecule called GTP into another molecule called GDP. GTPases play important roles in cell division, the process by which cells mature to carry out specific functions (differentiation), and the self-destruction of cells (apoptosis). The GTPases play important roles in several cell processes. The GTPases that are activated by alsin are involved in the proper placement of the various proteins and fats that make up the cell membrane, the transport of molecules from the cell membrane to the interior of the cell (endocytosis), and the development of specialized structures called axons and dendrites that project from neurons and are essential for the transmission of nerve impulses.

Health Conditions Related to Genetic Changes

[amyotrophic lateral sclerosis](#)

[infantile-onset ascending hereditary spastic paralysis](#)

At least 20 *ALS2* gene mutations have been found to cause infantile-onset ascending hereditary spastic paralysis. This disorder is characterized by progressive weakness and stiffness of muscles in the legs, arms, neck, and head that begins within the first 2 years of life. Mutations in the *ALS2* gene alter the instructions for making alsin, often resulting in the production of an abnormally short alsin protein that is unstable and rapidly broken down. It is unclear exactly how *ALS2* gene mutations cause infantile-onset ascending hereditary spastic paralysis. Research suggests that a lack of alsin and the subsequent loss of GTPase functions, such as endocytosis and the development of axons and dendrites, contribute to the progressive atrophy of motor neurons that is characteristic of this condition.

[juvenile primary lateral sclerosis](#)

Researchers have identified three mutations in the *ALS2* gene that cause juvenile primary lateral sclerosis, which is characterized by progressive weakness and

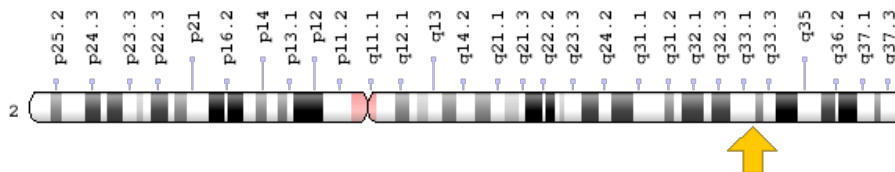
stiffness of muscles in the arms, legs, and face that typically begins in childhood. Two of the mutations that cause this disorder delete nucleotides, and one mutation replaces one nucleotide with an incorrect nucleotide. These mutations alter the instructions for producing alsin. As a result, alsin is unstable and is broken down rapidly by the cell, or it is disabled and cannot function properly.

It is unclear how the loss of functional alsin protein causes juvenile primary lateral sclerosis. Loss of alsin may result in a disruption of the movement of molecules within cells or impair the development of axons and dendrites. Researchers suggest that motor neurons and their long axons may be particularly vulnerable to changes in cell development. As a result, motor neuron function declines and eventually these nerve cells die, leading to the signs and symptoms of juvenile primary lateral sclerosis.

Chromosomal Location

Cytogenetic Location: 2q33.1, which is the long (q) arm of chromosome 2 at position 33.1

Molecular Location: base pairs 201,700,263 to 201,781,172 on chromosome 2 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ALS2_HUMAN
- ALS2CR6
- ALSJ
- amyotrophic lateral sclerosis 2 (juvenile)
- IAHSP
- KIAA1563
- PLSJ

Additional Information & Resources

Educational Resources

- Washington University, St. Louis Neuromuscular Disease Center
<http://neuromuscular.wustl.edu/synmot.html#cals>

GeneReviews

- ALS2-Related Disorders
<https://www.ncbi.nlm.nih.gov/books/NBK1243>
- Amyotrophic Lateral Sclerosis Overview
<https://www.ncbi.nlm.nih.gov/books/NBK1450>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ALS2%5BTIAB%5D%29+OR+%28alsin%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- ALSIN
<http://omim.org/entry/606352>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_ALS2.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=ALS2%5Bgene%5D>
- HGNC Gene Family: Rho guanine nucleotide exchange factors
<http://www.genenames.org/cgi-bin/genefamilies/set/722>
- HGNC Gene Family: VPS9 domain containing
<http://www.genenames.org/cgi-bin/genefamilies/set/928>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=443
- King's College London: Amyotrophic Lateral Sclerosis Online Genetics Database
http://alsod.iop.kcl.ac.uk/Als/Overview/gene.aspx?gene_id=ALS2

- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/57679>
- UniProt
<http://www.uniprot.org/uniprot/Q96Q42>

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